

PATENT COOPERATION TREATY

JS

From the INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing (day/month/year)	17 FEB 2006 1
FOR FURTHER ACTION See paragraphs 1 and 4 below	
International application No. PCT/IL04/00181	International filing date (day/month/year) 24 February 2004 (24.02.2004)

Applicant's or agent's file reference
27558

International application No.
PCT/IL04/00181

Applicant
METABOGAL, LTD

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70.

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☒ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☒ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/ US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
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Authorized officer

Manjunath N. Rao, Ph.D.

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[Signature]
for

PATENT COOPERATION TREATY

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 27558	FOR FURTHER ACTION		see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/IL04/00181	International filing date (<i>day/month/year</i>) 24 February 2004 (24.02.2004)	(Earliest) Priority Date (<i>day/month/year</i>) 27 April 2003 (27.04.2003)	
Applicant METABOGAL, LTD			

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 7 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the Report

a. With regard to the **language**, the international search was carried out on the basis of:



the international application in the language in which it was filed.



a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☒ **Unity of invention is lacking** (See Box No. III)

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. _____



as suggested by the applicant.



as selected by this Authority, because the applicant failed to suggest a figure.



as selected by this Authority, because this figure better characterizes the invention.

b. ☒ none of the figures is to be published with the abstract.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

a. type of material



a sequence listing



table(s) related to the sequence listing

b. format of material



on paper



in electronic form

c. time of filing/furnishing



contained in the international application as filed



filed together with the international application in electronic form



furnished subsequently to this Authority for the purposes of search

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
 2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
 3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: 1-24,28-31,33-37 and 42
 4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
- Remark on Protest**
- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
 - ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
 - ☐ No protest accompanied the payment of additional search fees.

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A. CLASSIFICATION OF SUBJECT MATTER IPC(8) : C12P 21/06; C12N 9/00, 9/14, 1/12, 1/20, 5/00, 15/00; C07H 21/04; A01H 11/00 US CL : 435/4, 6, 41, 69.1, 183, 195, 252.1, 252.3, 254.1, 320.1, 325, 410.; 536/23.1, 23.4, 23.5; 800/295 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 435/4, 6, 41, 69.1, 183, 195, 252.1, 252.3, 254.1, 320.1, 325, 410.; 536/23.1, 23.4, 23.5; 800/295 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/40686 (GENZYME CORP.) 23 May 2002 (23.05.2002), see entire document.	1-11, 28-31, 33-37, 42
X	WO 02/15927 (TRANSKARYOTRIC THERAPEUTICS INC.) 28 February 2002 (28.02.2002) see entire document.	1-11, 28-31, 33-37, 42
X	VAN WEELY et al. Function of oligosaccharide modification in glucocerebrosidase, a membrane-associated lysosomal hydrolase. Eur. J. Biochem., 1990, Vol. 191, No. 3, pages 669-677.	1-11, 28-31, 33-37, 42

Y		
X	MARTIN BM et al. Glycosylation and processing of high levels of active human glucocerebrosidase in invertebrate cells using a baculovirus expression vector. DNA, 1988, Vol. 7, No.2, pages 99-106.	1-11, 28-31, 33-37, 42
X	ERICKSON AH et al. Biosynthesis of lysosomal enzyme glucocerebrosidase. J. Biol. Chem., 1985, Vol. 260, No.26, pages 14319-14324.	1-11, 28-31, 33-37, 42
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents:		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"I" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E"	earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed	
Date of the actual completion of the international search 14 November 2005 (14.11.2005)		Date of mailing of the international search report 17 FEB 2006
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201		Authorized officer Manjunath N. Rao, Ph.D. Telephone No. 674-272-1600

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C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	Database GenBank, US National Library of Medicine, (Bethesda, MD, USA) No. AAR15823, BOLLER et al., March 2003.	16
X --- Y	Database GenBank, US National Library of Medicine, (Bethesda, MD, USA) No. ABP81239, ZHU T et al., February 2003.	16

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-24, drawn to host cell producing high mannose recombinant proteins comprising a polynucleotide encoding a recombinant protein and a signal for causing the recombinant to be produced as a high mannose protein.

Group II, claims 28-31, 33-37, 42, drawn to a recombinant high-mannose polypeptide.

Group III, claims 38-41, drawn to a recombinant high-mannose protein in a plant cell culture.

Group IV, claims 43-46, drawn to method of making high-mannose protein.

Group V, claims 57, drawn to a method of treating a disorder using the high mannose protein.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

According to PCT Rule 13.2 unity of invention exists only when the shared same or corresponding special technical feature is a contribution over the prior art. The inventions of Groups I-VI do not relate to a single general inventive concept because they lack the same or corresponding special technical feature. The technical feature of Groups I-V is a host cell producing a high-mannose recombinant protein comprising a polynucleotide encoding a recombinant protein and a signal sequence responsible for high-mannose content. Dunn-Coleman et al. WO 02/68666, dated 6 Sept. 2002 disclose such a host cell comprising a polynucleotide encoding an esterase polypeptide comprising a signal sequence. The reference does not specifically disclose that said polypeptide is a high-mannose polypeptide. However, since the signal sequence in the reference is a vacuolar signal sequence which is similar to the signal sequence herein, the Authorized Office takes the position that said host cell comprising said polynucleotide inherently encodes a polypeptide as a high-mannose polypeptide. Therefore, the invention when considered as a whole does not make a contribution over the prior art.

Furthermore, pursuant to 37 C.F.R. 1.475 (d), the ISA/US considers that where multiple products and processes are claimed, the main invention shall consist of the first invention of the category first mentioned in the claims and the first recited invention of each of the other categories related thereto. Accordingly, the main invention (Group I) comprises the first-recited product, a host cell. Further pursuant to 37 C.F.R. ' 1.475 (d), the ISA/US considers that any feature which the subsequently recited products and methods share with the main invention does not constitute a special

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technical feature within the meaning of PCT Rule 13.2 and that each of such products and methods accordingly defines a separate invention.

Claims 25-27, 32, 47-56, 58-72 have been found to be unsearchable under Article 17(2)(b) because of the defects under Article 17(2)(a). These claims are improper multiple dependent claims. Therefore they have not been included with any invention.

Continuation of B. FIELDS SEARCHED Item 3:

CAPLUS, BIOSIS, SCISEARCH, BIOTECHABS, BIOTECHDS, DGENE, PASCAL, CABA, LIFESCI, USPTO-
WEST, BIOTECHNO, GENBANK, AGRICOLA, EMBASE, MEDLINE, ESBIOBASE, FSTA,